Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Original) A conjugate comprising one or more bioactive components covalently attached to at least one linear or branched polyalkylene glycol, wherein said polyalkylene glycol does not comprise an alkoxyl group at any terminus and said polyalkylene glycol is attached to a single bioactive component at a single site on the polyalkylene glycol.

2. (Original) The conjugate of claim 1, wherein said conjugate is reduced or substantially reduced in antigenicity compared to a conjugate comprising the same bioactive component(s) linked at the same site or sites on the bioactive component(s) to the same number of polyalkylene glycols of the same size and linear or branched structure containing one or more terminal alkoxyl groups.

3. (Original) The conjugate of claim 1, wherein said linear or branched polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol) and a copolymer of ethylene oxide and propylene oxide.

4. (Original) The conjugate of claim 3, wherein said linear or branched polyalkylene glycol is a poly(ethylene glycol) ("PEG").

5. (Original) The conjugate of claim 1, wherein the attachment of said polyalkylene glycol to said bioactive component(s) is carried out using a reactive derivative of at least one polyalkylene glycol selected from the group consisting of linear dihydroxyPEGs ("PEG diols"), hydroxyPEG-monoacetals and hydroxyPEG-monoacids.

6. (Original) The conjugate of claim 1, wherein the attachment of said polyalkylene glycol to said bioactive component(s) is carried out using a reactive derivative of hydroxyPEG selected from the group consisting of a monoaldehyde, a monoester of a monoacid, a monoamine, a monothiol, a monodisulfide, a monobromophenyl carbonate,

a monochlorophenyl carbonate, a monofluorophenyl carbonate, a mononitrophenyl carbonate, a monocarbonylimidazole, a monohydrazide, a monocarbazate, a monoiodoacetamide, a monomaleimide, a monoorthopyridyl disulfide, a monooxime, a monophenyl glyoxal, a monothiazolidine-2-thione, a monothioester, a monotriazine and a monovinylsulfone.

7. (Original) The conjugate of claim 1, wherein said polyalkylene glycol has a molecular weight of from about 1,000 Daltons (1 kDa) to about 100,000 Daltons (100 kDa).

8. (Original) The conjugate of claim 7, wherein said polyalkylene glycol has a molecular weight of from about 2 kDa to about 60 kDa.

9. (Original) The conjugate of claim 8, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 2 kDa to about 30 kDa.

10. (Original) The conjugate of claim 9, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 5 kDa to about 20 kDa.

11. (Original) The conjugate of claim 8, wherein said polyalkylene glycol has a molecular weight of from about 10 kDa to about 20 kDa.

12. (Original) The conjugate of claim 11, wherein said polyalkylene glycol has a molecular weight of about 12 kDa.

13. (Original) The conjugate of claim 8, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 60 kDa.

14. (Original) The conjugate of claim 13, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 22 kDa.

15. (Original) The conjugate of claim 14 wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

16. (Original) The conjugate of claim 13, wherein said polyalkylene glycol has a molecular weight of about 27 kDa to about 33 kDa.

17. (Original) The conjugate of claim 1, wherein said conjugate comprises from about one to about 100 strands of said polyalkylene glycol.

18. (Original) The conjugate of claim 17, wherein said conjugate comprises from about one to about five strands of said polyalkylene glycol.

19. (Original) The conjugate of claim 18, wherein said conjugate comprises about one or about two strands of said polyalkylene glycol.

20. (Original) The conjugate of claim 17, wherein said conjugate comprises from about five to about 100 strands of said polyalkylene glycol.

21. (Original) The conjugate of claim 1, wherein said polyalkylene glycol is selected from the group consisting of a monohydroxyPEG-acid and a dihydroxyPEG-acid, such as dihydroxyPEG-lysine.

22. (Original) The conjugate of claim 1, wherein said polyalkylene glycol, if linear, has a hydroxyl group at the terminus that is not attached to the bioactive component(s) ("the distal terminus") or, if branched, has a hydroxyl group at every distal terminus.

23. (Original) The conjugate of claim 5, wherein said polyalkylene glycol is a reactive derivative of said linear dihydroxyPEG.

24. (Original) The conjugate of claim 5, wherein said polyalkylene glycol is a reactive derivative of said hydroxyPEG-monocarboxylic acid.

25. (Original) The conjugate of claim 1, wherein said bioactive component is selected from the group consisting of a peptide, a protein, a glycoprotein, an organic compound, an amine-containing compound, a carboxyl-containing compound, a hydroxyl-containing compound and a thiol-containing compound.

26. (Original) The conjugate of claim 25, wherein said bioactive component is selected from the group consisting of a peptide, a protein and a glycoprotein.

27. (Original) The conjugate of claim 26, wherein said peptide or protein or

glycoprotein is selected from the group consisting of an enzyme, a serum protein, a serum glycoprotein, a blood cell protein, a pigmentary protein, hemoglobin, a viral protein, a peptide hormone, a protein hormone, a glycoprotein hormone, a hypothalamic releasing factor, a cytokine, a growth factor and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing group.

28. (Original) The conjugate of claim 27, wherein said serum protein is selected from the group consisting of an albumin, an immunoglobulin, a blood clotting factor and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing serum proteins.

29. (Original) The conjugate of claim 27, wherein said peptide hormone or protein hormone or glycoprotein hormone is selected from the group consisting of an antidiuretic hormone, chorionic gonadotropin, luteinizing hormone, follicle-stimulating hormone, insulin, prolactin, a somatomedin, growth hormone, thyroid-stimulating hormone, a placental lactogen and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing hormones.

30. (Original) The conjugate of claim 27, wherein said growth factor is selected from the group consisting of a colony-stimulating factor, an epidermal growth factor, a fibroblast growth factor, an insulin-like growth factor, a transforming growth factor, a platelet-derived growth factor, a nerve growth factor, a hepatocyte growth factor, a neurotrophic factor, a ciliary neurotrophic factor, a brain-derived neurotrophic factor, a glial-derived neurotrophic factor or a bone morphogenic peptide and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing growth factors.

31. (Original) The conjugate of claim 27, wherein said cytokine is selected from the group consisting of erythropoietin, a lymphokine, an interleukin, an interferon, a tumor necrosis factor, a leukemia inhibitory factor and thrombopoietin, and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing cytokines.

32. (Original) The conjugate of claim 27, wherein said enzyme is selected from

the group consisting of a carbohydrate-specific enzyme, a proteolytic enzyme, an oxidoreductase, a transferase, a hydrolase, a lyase, an isomerase and a ligase.

33. (Original) The conjugate of claim 32, wherein said oxidoreductase enzyme is a uricase.

34. (Original) The conjugate of claim 32, wherein said proteolytic enzyme is a plasminogen activator.

35. (Original) The conjugate of claim 26, wherein said peptide, protein or glycoprotein is an allergen.

36. (Original) The conjugate of claim 1, wherein said bioactive compound is a taxane or a derivative thereof.

37. (Original) The conjugate of claim 1, wherein said bioactive compound is an antibiotic or a derivative thereof.

38. (Original) A pharmaceutical composition comprising the conjugate of claim 1 and a pharmaceutically acceptable excipient or carrier.

39. - 58. (Canceled)

59. (Currently amended) A conjugate comprising one or more bioactive components covalently attached to at least one linear or branched polyalkylene glycol activated at only one terminus ("a monoactivated polyalkylene glycol") produced by ~~the method of claim 54~~ a method comprising:

(a) obtaining a polyalkylene glycol that does not contain any end group that is a stably linked alkoxyl group;

(b) optionally, prior to the conversion of the polyalkylene glycol of (a) to a monofunctionally activated polyalkylene glycol, protecting all except one of the end groups by the addition of one or more removable blocking groups, such as *t*-butoxyl group(s), aryloxyl group(s) or triphenylmethyl group(s) ("trityl group(s)");

(c) producing a monofunctionally activated derivative of said polyalkylene glycol by reacting said polyalkylene glycol with a derivatizing compound or

compounds under conditions such that said polyalkylene glycol is derivatized with a single derivatizing group at an end that does not contain said removable blocking group or groups;

(d) if a blocking group was added to protect the end group(s), as described in (b) above, removing said blocking group, in one or more steps, without removing the activating group attached as described in (c) above, to produce a monofunctionally activated polyalkylene glycol wherein the distal terminus or distal termini are hydroxyl groups; and

(e) contacting said monofunctionally activated polyalkylene glycol with at least one bioactive component, under conditions that favor the covalent binding of said monofunctionally activated polyalkylene glycol to said bioactive component, or

(f) alternatively, performing (e) above prior to performing (d) above.

60. (Original) The conjugate of claim 59, wherein said conjugate is reduced or substantially reduced in antigenicity compared to a conjugate comprising the same bioactive component linked at the same site or sites on the bioactive component to the same number of molecules of polyalkylene glycol of the same size and linear or branched structure that contain an alkoxyl group at the distal terminus, if the polyalkylene glycol is linear, or contain two or more alkoxyl groups at the distal termini, if the polyalkylene glycol is branched.

61. (Original) The conjugate of claim 59, wherein said polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol) and a copolymer of ethylene oxide and propylene oxide.

62. (Original) The conjugate of claim 59, wherein the polyalkylene glycol component is selected from the group consisting of a linear poly(ethylene glycol) and a branched poly(ethylene glycol).

63. (Original) The conjugate of claim 59, wherein each said polyalkylene glycol has a molecular weight of from about 1 kDa to about 100 kDa.

64. (Original) The conjugate of claim 63, wherein said polyalkylene glycol has a molecular weight of from about 2 kDa to about 60 kDa.

65. (Original) The conjugate of claim 64, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 2 kDa to about 30 kDa.

66. (Original) The conjugate of claim 65, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 5 kDa to about 20 kDa.

67. (Original) The conjugate of claim 64, wherein said polyalkylene glycol has a molecular weight of from about 10 kDa to about 20 kDa.

68. (Original) The conjugate of claim 67, wherein said polyalkylene glycol has a molecular weight of about 12 kDa.

69. (Original) The conjugate of claim 64, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 60 kDa.

70. (Original) The conjugate of claim 69, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 22 kDa.

71. (Original) The conjugate of claim 70, wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

72. (Original) The conjugate of claim 69, wherein said polyalkylene glycol has a molecular weight of about 27 kDa to about 33 kDa.

73. (Original) The conjugate of claim 59, wherein said conjugate comprises from one to about 100 strands of said polyalkylene glycol.

74. (Original) The conjugate of claim 73, wherein said conjugate comprises from about one to about five strands of said polyalkylene glycol.

75. (Original) The conjugate of claim 74, wherein said conjugate comprises about one or about two strands of said polyalkylene glycol.

76. (Original) The conjugate of claim 73, wherein said conjugate comprises about five to about 100 strands of said polyalkylene glycol.

77. (Original) The conjugate of claim 59, wherein the monofunctionally activated polyalkylene glycol used in the synthesis of said conjugate is selected from the group consisting of a hydroxyPEG-monoaldehyde and a reactive ester of a hydroxyPEG-monoacid.

78. (Original) The conjugate of claim 59, wherein the monofunctionally activated polyalkylene glycol used in the synthesis of said conjugate has a hydroxyl group at its distal terminus, if it is linear, or has a hydroxyl group at every distal terminus, if it is branched.

79. (Original) The conjugate of claim 59, wherein the monofunctionally activated polyalkylene glycol used in its synthesis is derived from a linear dihydroxyPEG.

80. (Original) The conjugate of claim 59, wherein the bioactive component is selected from the group consisting of a peptide, a protein, a glycoprotein, an organic compound, an amine-containing compound, a carboxyl-containing compound, a hydroxyl-containing compound and a thiol-containing compound.

81. (Original) The conjugate of claim 80, wherein said bioactive component is selected from the group consisting of a peptide, a protein and a glycoprotein.

82. (Original) The conjugate of claim 81, wherein said peptide or protein or glycoprotein is selected from the group consisting of an enzyme, a serum protein, a serum glycoprotein, a blood cell protein, a pigmentary protein, hemoglobin, a viral protein, a peptide hormone, a protein hormone, a glycoprotein hormone, a hypothalamic releasing factor, a cytokine, a growth factor and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing group.

83. (Original) The conjugate of claim 82, wherein said serum protein is selected from the group consisting of an albumin, an immunoglobulin, a blood-clotting factor and peptides and proteins and glycoproteins that mimic or function as antagonists of any of

the foregoing serum proteins.

84. (Original) The conjugate of claim 82, wherein said peptide hormone or protein hormone or glycoprotein hormone is selected from the group consisting of an antidiuretic hormone, chorionic gonadotropin, luteinizing hormone, follicle-stimulating hormone, insulin, prolactin, a somatomedin, growth hormone, thyroid-stimulating hormone, a placental lactogen and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing hormones.

85. (Original) The conjugate of claim 82, wherein said growth factor is selected from the group consisting of a colony-stimulating factor, an epidermal growth factor, a fibroblast growth factor, an insulin-like growth factor, a transforming growth factor, a platelet-derived growth factor, a nerve growth factor, a hepatocyte growth factor, a neurotrophic factor, a ciliary neurotrophic factor, a brain-derived neurotrophic factor, a glial-derived neurotrophic factor or a bone morphogenic peptide and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing growth factors.

86. (Original) The conjugate of claim 82, wherein said cytokine is selected from the group consisting of erythropoietin, a lymphokine, an interleukin, an interferon, a tumor necrosis factor, a leukemia inhibitory factor and thrombopoietin, and peptides and proteins and glycoproteins that mimic or function as antagonists of any of the foregoing cytokines.

87. (Original) The conjugate of claim 82, wherein said enzyme is selected from the group consisting of a carbohydrate-specific enzyme, a proteolytic enzyme, an oxidoreductase, a transferase, a hydrolase, a lyase, an isomerase and a ligase.

88. (Original) The conjugate of claim 87, wherein said oxidoreductase enzyme is a uricase.

89. (Original) The conjugate of claim 87, wherein said proteolytic enzyme is a plasminogen activator.

90. (Original) The conjugate of claim 81, wherein said peptide, protein or glycoprotein is an allergen.

91. (Original) The conjugate of claim 59, wherein the bioactive compound is a taxane or a derivative thereof.

92. (Original) The conjugate of claim 59, wherein said bioactive compound is an antibiotic or a derivative thereof.

93. (Original) A pharmaceutical composition comprising the conjugate of claim 59 and a pharmaceutically acceptable excipient or carrier.

94. (Original) A kit comprising the conjugate of claim 1.

95. (Original) A kit comprising the pharmaceutical composition of claim 38.

96. (Original) A kit comprising the conjugate of claim 59.

97. - 100. (Canceled)

101. (New) The conjugate of claim 27, wherein said growth factor is a colony-stimulating factor.

102. (New) The conjugate of claim 101, wherein said colony-stimulating factor is a granulocyte-macrophage colony stimulating factor (GM-CSF); a fragment, variant or derivative thereof; or a peptide, protein or glycoprotein that mimics GM-CSF.

103. (New) The conjugate of claim 102, wherein said GM-CSF, fragment, variant or derivative thereof, or peptide, protein or glycoprotein that mimics GM-CSF, is covalently attached to one linear or branched polyalkylene glycol molecule that does not comprise an alkoxyl group at any terminus and that is attached to a single molecule of said GM-CSF.

104. (New) The conjugate of claim 102, wherein said GM-CSF, fragment, variant or derivative thereof, or peptide, protein or glycoprotein that mimics GM-CSF, is covalently attached to two linear or branched polyalkylene glycol molecules that do not

comprise an alkoxyl group at any terminus and that are attached to a single molecule of said GM-CSF.

105. (New) The conjugate of claim 82, wherein said growth factor is a colony-stimulating factor.

106. (New) The conjugate of claim 105, wherein said colony-stimulating factor is a granulocyte-macrophage colony stimulating factor (GM-CSF); a fragment, variant or derivative thereof; or a peptide, protein or glycoprotein that mimics GM-CSF.

107. (New) The conjugate of claim 106, wherein said GM-CSF, fragment, variant or derivative thereof, or peptide, protein or glycoprotein that mimics GM-CSF, is covalently attached to one linear or branched polyalkylene glycol molecule that does not comprise an alkoxyl group at any terminus and that is attached to a single molecule of said GM-CSF.

108. (New) The conjugate of claim 106, wherein said GM-CSF, fragment, variant or derivative thereof, or peptide, protein or glycoprotein that mimics GM-CSF, is covalently attached to two linear or branched polyalkylene glycol molecules that do not comprise an alkoxyl group at any terminus and that are attached to a single molecule of said GM-CSF.